

034404-001

VITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Pierre Falson et al.

Filing Date:

Sir:

Application No.: 10/528,344

March 18, 2005

Group Art Unit:

Examiner:

Confirmation No.:

Title: 'SYSTEMS FOR EXPRESSING TOXIC PROTEINS, VECTORS AND METHOD OF PRODUCING

TOXIC PROTEINS

FIRST INFORMATION DISCLOSURE STATEMENT TRANSMITTAL LETTER

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

	closed is a 49 for the above	FIRST e-identified pater		sclosure Statement and	d accompanying form
	The fee of \$18 A statement up A statement up § 1.17(p) are a Charge A check in the	30.00 (1806) as nder 37 C.F.R. { nder 37 C.F.R. { also enclosed to Depo	§ 1.97(e) is also ereget is also ereget is and the osit Account No. 02	F.R. § 1.17(p) is also e nclosed.	as set forth in 37 C.F.R
1.21 tha		ed by this paper			C.F.R. §§ 1.16, 1.17 and sit Account No. 02-4800.
			Res	pectfully submitted,	
			BU	RNS, DOANE, SWECK	ŒR & MATHIS, L.L.P.
P.O. Bo Alexand (703) 83	Iria, Virginia 223	13-1404	Ву	ml.m.lle	z.l.
Date:	Tu. 23.	225		Melissa M. Hayworth	774

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FIRST INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56, the accompanying information is being submitted in accordance with 37 C.F.R. §§ 1.97 and 1.98.

Pursuant to 37 C.F.R. § 1.98, a copy of each of the documents cited is enclosed.

The documents are being submitted within three (3) months of the filing or entry of the national stage of this application or before the first Office Action on the merits, whichever is later. Since these documents are being filed within the time period set forth in 37 C.F.R. § 1.97(b), no fee or statement is required.

Five of the documents being disclosed were cited in a search report from French Application 0211676 dated June 12, 2003, a copy of which is enclosed.

To assist the Examiner, the documents are listed on the attached form PTO-1449. It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date Jun 23, 2005

Melissa M. Hayworth

Registration No. 45,774

P.O. Box 1404 Alexandria, Virginia 22313-1404 (703) 836-6620

Substitute for form 1449A/PTO & 1449B/PTO			Com	Complete if Known			
	F	IRST 🛖	Application Number	10. 344			
INFO	DRMATIC	N DISCLOSURE	Filing Date	March 18, 2005			
STA	TEMENT	BY APPLICANT	First Named Inventor	Pierre Falson et al.			
	(use as many	sheets as necessary)	Examiner Name				
Sheet 1 pf C 2		A 0 1 62	Attorney Docket Number	034404-001			
		5					
		JUN 2 3 2005 2	U.S. PATENT DOCUMENTS				
Examiner Initials	Document Number	Kind Code			Issue/Publication Date (MM-DD-YYYY)		

FOREIGN PATENT DOCUMENTS											
	•						ST	ATUS			_
Examiner Initials	Document Number	Kind Code (if known)	Country	Date of Publication (MM-DD-YYYY)	Translation	Partial Translation	Eng. Lang. Summary	Search Report	IPER	Abstract	Spec

(MM-DD-YYYY)

NON-PATENT LITERATURE DOCUMENTS						
Examiner Initials	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.					
	Search Report from French Application 0211676 dated June 12, 2003.					
-	Wang, Y, et al., "A unique approach for high level expression and production of a recombinant cobra neurotoxin in <i>Escherichia coli</i> ", <i>Journal of Biotechnology</i> Vol. 94 No. 3:235-244 (2002).					
	Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in <i>E. coli</i> Cells", <i>Virology</i> 250 :1-8 (1998).					
_	Ciccaglione, A.R., et al., "Secretion and purification of HCV E1 protein forms as glutathione-S-transferase fusion in the baculovirus insect cell system", <i>Virus Research</i> 55 :157-165 (1998).					
-	Okamoto, H., et al., "The 5'-terminal sequence of the hepatitis C virus genome", abstract from EMBL GenBank DDBJ databases, February, 1992.					
-	Sarrazin, C., et al., "Quasispecies heterogeneity of the carboxyterminal part of the E2 gene including the PePHD and sensitivity of hepatitis C virus 1b isolates to antiviral therapy", abstract from EMBL GenBank DDBJ databases, July 2001.					
	Christendat, D., et al., "Structural proteomics: prospects for high throughput sample preparation", <i>Progress in Biophysics & Molecular Biology</i> 73 :339-345 (2000).					
	Hammarström, M., et al., "Rapid screening for improved solubility of small human proteins produces as fusion proteins in <i>Escherichia coli</i> ", <i>Protein Science</i> 11:313-321 (2002).					
	Elble, R., "An Efficient Procedure to Dialyze Volumes in the Range of 10-200 μl", <i>Biotechniques</i> 13 (1) (1992).					
	Falson, P., "Improved Phenol-Based Method for the Isolation of DNA Fragments from Low Melting Temperature-Agarose Gels", Biotechniques 13 (1):20-22 (1992).					
	Falson, P, et al., "Functional Nucleotide-Binding Domain in the F_0 - F_1 -ATPsynthase α Submit from the Yeast Schizosaccharomyces pombe", Biochemistry 32 :10387-10397 (1993).					
_	Ciccaglione, A.R., et al., "Expression and Membrane Association of Hepatitis C Virus Envelope 1 Protein", Virus Genes 21 (3):223-226 (2000).					
	Sisk, W.P., et al., "Deletion of hydrophobic domains of viral glycoproteins increases the level of their production in <i>Escherichia coli</i> ", <i>Gene</i> 112 :157-162 (1992).					
	Paulsen, I.T., et al., "Unified inventory of established and putative transporters encoded within the complete genome of Saccharomyces cerevisiae", FEBS Letters 430:116-125 (1998).					

Examiner		Date
Signature		Considered
AEN ARRIVED	1 111 1 11 1	

Substitute for form 1449A/PTO & 1449B/PTO	Con	nplete if Known		
FIRST	Application Number	10/		
INFORMATION DISCLOSURE	Filing Date	March 18, 2005		
STATEMENT BY APPLICANT	First Named Inventor	Pierre Falson et al.		
ase as many smalls as necessary)	Examiner Name			
Sheet 2 of 2	Attorney Docket Number	034404-001		
JUN 2 3 2005 5 NON-PAT	TENT LITERATURE DOCUMENTS			
Examiner Initials Ini	TERS), title of the article (when appropriage(s), volume-issue number(s), public	riate), title of the item (book, magazine, journal, sher, city and/or country where published.		
		", nature genetics 15 :137-145 (1997).		
Arechaga, I., "Characterization of new over-production of the b subunit of F ₁		cherichia coli accompanying large scale s 482:215-219 (2000)		
Miroux B and Walker J F "Over-pro	oduction of Proteins in Escherici	hia coli: Mutant Hosts that Allow		

Decottignies A., et al., "Complete inventory of the yeast ABC proteins", nature genetics 15:137-145 (1997). Arechaga, I., "Characterization of new intracellular membranes in Escherichia coli accompanying large sca over-production of the b subunit of F ₁ F ₆ ATP synthase", FEBS Letters 482:215-219 (2000) Miroux, B. and Walker, J.E., "Over-production of Proteins in Escherichia coli: Mutant Hosts that Allow Synthesis of some Membrane Proteins and Globular Proteins at High Levels", J. Mol. Biol. 260:289-298 (1996). Mayo, M.A. and Pringle, C.R., "Virus Taxonomy", Journal of General Virology 79:649-657 (1998). De Beeck, A.O., et al., "The Transmembrane Domains of Hepatitis C Virus Envelope Glycoproteins E1 and E2 Play a Major Role in Heterodimerization", The Journal of Chemistry 275(40):31428-31437 (2000). Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome", Science 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in E coli Cells", Virology 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", Journal of General Virology 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster and Homo sapiens; a review of the considerable within-species diversity" Nucleic Acids Research 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction", Methods in Enzymology 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", Proc. Natl. Acad. Sci., USA 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in Escherichia coli: An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transfera		NON-PATENT LITERATURE DOCUMENTS
Arechaga, I., "Characterization of new intracellular membranes in <i>Escherichia coli</i> accompanying large sca over-production of the b subunit of F ₁ F ₆ ATP synthase", <i>FEBS Letters</i> 482:215-219 (2000) Miroux, B. and Walker, J.E., "Over-production of Proteins in <i>Escherichia coli</i> : Mutant Hosts that Allow Synthesis of some Membrane Proteins and Globular Proteins at High Levels", <i>J. Mol. Biol.</i> 260:289-298 (1996). Mayo, M.A. and Pringle, C.R., "Virus Taxonomy", <i>Journal of General Virology</i> 79:649-657 (1998). De Beeck, A.O., et al., "The Transmembrane Domains of Hepatitis C Virus Envelope Glycoproteins E1 and E2 Play a Major Role in Heterodimerization", <i>The Journal of Chemistry</i> 275(40):31428-31437 (2000). Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Biood-Borne Non-A, Non-B Viral Hepatitis Genome", <i>Science</i> 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in <i>Ecoli</i> Cells", <i>Virology</i> 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", <i>Journal of General Virology</i> 32:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe</i> , <i>Drosophila melanogaster</i> and <i>Homo sapiens</i> , a review of the considerable within-species diversity" <i>Nucleic Acids Research</i> 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA <i>in Vitro</i> via a Polymerase-Catalyzed Chain Reaction", <i>Methods in Enzymology</i> 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci., USA</i> 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli</i> : An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. and		blude name of a author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, posium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
Arechaga, I., "Characterization of new intracellular membranes in <i>Escherichia coli</i> accompanying large sca over-production of the b subunit of F ₁ F ₆ ATP synthase", <i>FEBS Letters</i> 482:215-219 (2000) Miroux, B. and Walker, J.E., "Over-production of Proteins in <i>Escherichia coli</i> : Mutant Hosts that Allow Synthesis of some Membrane Proteins and Globular Proteins at High Levels", <i>J. Mol. Biol.</i> 260:289-298 (1996). Mayo, M.A. and Pringle, C.R., "Virus Taxonomy", <i>Journal of General Virology</i> 79:649-657 (1998). De Beeck, A.O., et al., "The Transmembrane Domains of Hepatitis C Virus Envelope Glycoproteins E1 and E2 Play a Major Role in Heterodimerization", <i>The Journal of Chemistry</i> 275(40):31428-31437 (2000). Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Biood-Borne Non-A, Non-B Viral Hepatitis Genome", <i>Science</i> 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in <i>Ecoli</i> Cells", <i>Virology</i> 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", <i>Journal of General Virology</i> 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe</i> , <i>Drosophila melanogaster</i> and <i>Homo sapiens</i> , a review of the considerable within-species diversity" <i>Nucleic Acids Research</i> 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA <i>in Vitro</i> via a Polymerase-Catalyzed Chain Reaction", <i>Methods in Enzymology</i> 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 TRNA polymerase/promoter system for controlled exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci., USA</i> 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli</i> : An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathinore S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. an	•	Decottignies A., et al., "Complete inventory of the yeast ABC proteins", <i>nature genetics</i> 15 :137-145 (1997).
Synthesis of some Membrane Proteins and Globular Proteins at High Levels", <i>J. Mol. Biol.</i> 260:289-298 (1996). Mayo, M.A. and Pringle, C.R., "Virus Taxonomy", <i>Journal of General Virology</i> 79:649-657 (1998). De Beeck, A.O., et al., "The Transmembrane Domains of Hepatitis C Virus Envelope Glycoproteins E1 and E2 Play a Major Role in Heterodimerization", <i>The Journal of Chemistry</i> 275(40):31428-31437 (2000). Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome", <i>Science</i> 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in <i>E coli</i> Cells", <i>Virology</i> 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", <i>Journal of General Virology</i> 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe</i> , <i>Drosophila melanogaster</i> and <i>Homo sapiens</i> ; a review of the considerable within-species diversity" <i>Nucleic Acids Research</i> 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA <i>in Vitro</i> via a Polymerase-Catalyzed Chain Reaction", <i>Methods in Enzymology</i> 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci.</i> , USA 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli</i> : An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" <i>Analytical Biochemistry</i> 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", <i>Current Protocols</i> Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dod	-	Arechaga, I., "Characterization of new intracellular membranes in Escherichia coli accompanying large scale
De Beeck, A.O., et al., "The Transmembrane Domains of Hepatitis C Virus Envelope Glycoproteins E1 and E2 Play a Major Role in Heterodimerization", <i>The Journal of Chemistry</i> 275(40):31428-31437 (2000). Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome", <i>Science</i> 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in <i>E coli</i> Cells", <i>Virology</i> 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", <i>Journal of General Virology</i> 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe</i> , <i>Drosophila melanogaster</i> and <i>Homo sapiens</i> ; a review of the considerable within-species diversity" <i>Nucleic Acids Research</i> 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA <i>in Vitro</i> via a Polymerase-Catalyzed Chain Reaction", <i>Methods in Enzymology</i> 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci., USA</i> 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli</i> : An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" <i>Analytical Biochemistry</i> 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", <i>Current Protocols</i> Supplement 1 Unit 16:2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", <i>Analytical Biochemistry</i> 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins dur		Synthesis of some Membrane Proteins and Globular Proteins at High Levels", J. Mol. Biol. 260:289-298
E2 Play a Major Role in Heterodimerization", <i>The Journal of Chemistry</i> 275(40):31428-31437 (2000). Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome", <i>Science</i> 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in <i>Ecoli</i> Cells", <i>Virology</i> 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", <i>Journal of General Virology</i> 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe</i> , <i>Drosophila melanogaster and Homo sapiens</i> ; a review of the considerable within-species diversity" <i>Nucleic Acids Research</i> 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA <i>in Vitro</i> via a Polymerase-Catalyzed Chain Reaction", <i>Methods in Enzymology</i> 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci., USA</i> 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli</i> : An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" <i>Analytical Biochemistry</i> 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", <i>Current Protocols</i> Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", <i>Analytical Biochemistry</i> 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", <i>Nature</i> 227:680-685 (1970). Sambrook, et al., "Expre	_	
Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome", Science 244:359-362 (1989). Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in E. coli Cells", Virology 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", Journal of General Virology 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster and Homo sapiens; a review of the considerable within-species diversity" Nucleic Acids Research 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction", Methods in Enzymology 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", Proc. Natl. Acad. Sci., USA 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in Escherichia coli: An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", Analytical Biochemistry 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" Analytical Biochemistry 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989).	/	De Beeck, A.O., et al., "The Transmembrane Domains of Hepatitis C Virus Envelope Glycoproteins E1 and E2 Play a Major Role in Heterodimerization", <i>The Journal of Chemistry</i> 275 (40):31428-31437 (2000).
Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in E. coli Cells", Virology 250:1-8 (1998). De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", Journal of General Virology 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster and Homo sapiens; a review of the considerable within-species diversity" Nucleic Acids Research 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction", Methods in Enzymology 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", Proc. Natl. Acad. Sci., USA 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in Escherichia coli: An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", Analytical Biochemistry 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" Analytical Biochemistry 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Choo, Q.L., et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis
De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", <i>Journal of General Virology</i> 82:2589-2595 (2001). Sharp, P.M., et al., "Codon usage patterns <i>Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe, Drosophila melanogaster</i> and <i>Homo sapiens</i> ; a review of the considerable within-species diversity" <i>Nucleic Acids Research</i> 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA <i>in Vitro</i> via a Polymerase-Catalyzed Chain Reaction", <i>Methods in Enzymology</i> 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci., USA</i> 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli:</i> An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" <i>Analytical Biochemistry</i> 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", <i>Current Protocols</i> Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", <i>Analytical Biochemistry</i> 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", <i>Nature</i> 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in <i>Escherichia coli</i> ", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Ciccaglione, A.R., et al., "Hepatitis C Virus E1 Protein Induces Modification of Membrane Permeability in E.
Sharp, P.M., et al., "Codon usage patterns Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster and Homo sapiens; a review of the considerable within-species diversity" Nucleic Acids Research 16(17):8207-8211 (1988). Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction", Methods in Enzymology 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", Proc. Natl. Acad. Sci., USA 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in Escherichia coli: An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", Analytical Biochemistry 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" Analytical Biochemistry 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	1	De Beeck, A.O., et al., "Biogenesis of hepatitis C virus envelope glycoproteins", Journal of General Virology
Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction", Methods in Enzymology 155:335-350 (1987). Tabor, S. and Richardson, C.C., "A bacteriophase T7 RNA polymerase/promoter system for controlled exclusive expression of specific genes", Proc. Natl. Acad. Sci., USA 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in Escherichia coli: An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", Analytical Biochemistry 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" Analytical Biochemistry 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	1	Sharp, P.M., et al., "Codon usage patterns Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster and Homo sapiens; a review of the considerable
exclusive expression of specific genes", <i>Proc. Natl. Acad. Sci., USA</i> 82:1074-1078 (1985). Guan, K.L., and Dixon, J.E., "Eukaryotic Proteins Expressed in <i>Escherichia coli</i> : An Improved Thrombin Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", <i>Analytical Biochemistry</i> 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" <i>Analytical Biochemistry</i> 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", <i>Current Protocols</i> Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", <i>Analytical Biochemistry</i> 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", <i>Nature</i> 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in <i>Escherichia coli</i> ", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Mullis, K.B. and Faloona, F.A., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction", Methods in Enzymology 155:335-350 (1987).
Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", Analytical Biochemistry 192:262-267 (1991). Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" Analytical Biochemistry 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	1	exclusive expression of specific genes", Proc. Natl. Acad. Sci., USA 82:1074-1078 (1985).
Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria" Analytical Biochemistry 202:293-298 (1992). Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Cleavage and Purification Procedure of Fusion Proteins with Glutathione S-Transferase", Analytical
Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 1 / Unit 16.2 (1990) Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", Analytical Biochemistry 166:368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Hakes, D.J. and Dixon, J.E., "New Vectors for High Level Expression of Recombinant Proteins in Bacteria", Analytical Biochemistry 202:293-298 (1992).
Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for the Separation of Proteins in the Range from 1 to 100 kDa", <i>Analytical Biochemistry</i> 166 :368-379 (1987). Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", <i>Nature</i> 227 :680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in <i>Escherichia coli</i> ", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Tabor, S., "Expression Using the T7 RNA Polymerase/Promoter System", Current Protocols Supplement 11
Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4", Nature 227:680-685 (1970). Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	/	Schägger, H. and von Jagow, G., "Tricine-Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis for
Sambrook, et al., "Expression of Cloned Genes in <i>Escherichia coli</i> ", Chapter 17, A laboratory manual, second edition, Cold Spring Harbor Laboratory Press (1989). "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	1	Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophase T4",
, "Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,	(Sambrook, et al., "Expression of Cloned Genes in Escherichia coli", Chapter 17, A laboratory manual,
	("Detection and Analysis of Proteins Expressed from Cloned Genes", Chapter 18, A laboratory manual,

Examiner	Date	
Signature	Considered	